REMARKS/ARGUMENTS

Claims 28-30 and 52-69 are presently pending. Claims 28-30 have been amended. No new matter is entered upon entry of these amendments. Claims 1-27 and 31-33 were previously canceled. Claims 34-51 were previously canceled and reinstated as claims 52-69.

I. Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 28-30 and 52-69 continue to stand rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. Applicant continues to traverse this rejection for all of the reasons of record, and respectfully requests reconsideration in view of the amendments made to the claims and the following remarks.

Entered SDS 7-21-04

A. The State of the Antisense Therapy Art Was Enabled as of the Priority Date

The positive results from Genta Inc.'s phase III clinical trials of the antisense drug, Genasense™, demonstrates that antisense technology indeed works *in vivo*, which refutes the Examiner's position that antisense is a highly unpredictable art. Given that Genta announced its results on 10 September 2003, the Office now questions whether the present invention is enabled as of 14 July 1998, the earliest priority date sought. While the results of the phase III clinical trials were only made in 2003, those trials were actually started years earlier. Indeed, the results of the very first phase I clinical trial of G3139 (oblimersen, Genasense™) in patients with non-Hodgkin's lymphoma (NHL) was reported in **1997** (see Hayes, D.F., "*Bcl-2 inhibition in the treatment of cancer: clinical studies with the Bcl-2 antisense oligonucleotide G3139*", in Beyond Chemotherapy, Emerging Targeted Therapies for the Treatment of Cancer, Symposium Proceedings, San Francisco, California, May 11, 2001, pages 12-18, the "Hayes reference", provided herewith as Exhibit A; citing Webb A., *et al. BCL-2 antisense therapy in patients with non-Hodgkin's lymphoma,* The Lancet, **1997 Apr 19**;349(9059):1137-1141, "the Webb reference", provided herewith as Exhibit B). According to the Hayes reference, among 21 patients treated with G3139, there was one complete response, two minor responses, and nine patients with stable diseases:

Single-Agent G3139

The initial phase I trial of G3139 evaluated single-agent therapy in patients with relapsed NHL.[4,5] G3139 was administered for 14 days by continuous subcutaneous infusion as a single course of therapy. Only 1 course of therapy was planned, but responding patients could be considered for a second treatment course. A total of 21 patients were enrolled, and G3139 doses were escalated from 4.6 to 195.8 mg/m2/d. Three patients received 2 courses of therapy.

Although all patients experienced inflammation at the infusion site, no significant systemic toxicities were noted until doses exceeded 110.4 mg/m2/d. The maximum tolerated dose was 147.2 mg/m2/d (4 mg/kg/d), and dose-limiting toxicities included thrombocytopenia, hypotension, fever, and asthenia. **Among the 21 patients, there were 1 complete response, 2 minor responses, and 9 patients with stable disease.** Correlative laboratory studies of tumor cells derived from peripheral blood, bone marrow, or lymph nodes indicated down-regulation of Bcl-2 protein in 7 of 16 samples.

Overall, treatment with G3139 was found to be tolerable, with antitumor activity suggested in patients with relapsed NHL. Laboratory evaluation confirmed that therapy with G3139 could affect downregulation of Bcl-2 production at clinically achievable concentrations.

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4. Webb A., et al., *BCL-2 antisense therapy in patients with non-Hodgkin's lymphoma,* The Lancet, 1997; 349: 1137-1141.

5. Waters J.S., et al., *Phase I clinical and pharmacokinetic study of bcl-2 antisense oligonucleotide therapy in patients with non-Hodgkin's lymphoma.* J. Clin. Oncol. 2000; 18: 1812-1823.

These results establish that patients with non-Hodgkin's lymphoma could be successfully treated with antisense technology on or before 19 April 1997, the publication date of the Webb reference. Thus, antisense therapy was already advanced to such an extent in 1997 that those skilled in the art could successfully treat humans with antisense technology. Because the art-skilled having the benefit of Applicant's specification could indeed make and use the claimed compounds to treat an organism at the time of the earliest priority date sought, the instant rejection under 35 U.S.C. § 112, first paragraph, is improper and should be withdrawn.

B. Claim Amendments Made to Advance Prosecution

The Office Action alleges that the ordinary and plain meaning of the words "treating an organism having a disease" in the preambles of claims 28-30 include treatment of an organism having a disease and administering a treatment to such an organism (page 4, lines 12-15). Although Applicant does not necessarily agree that these words carry this meaning, claims 28-30 have been amended in order to advance prosecution.

Conclusions:

Applicant requests the Examiner to:

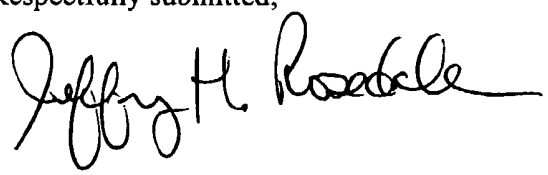
(1) enter the amendments to claims 28-30;

(2) reconsider and withdraw the rejection of the claims; and

(3) pass claims 28-30 and 52-69 to allowance.

If the Examiner is of contrary view, the Examiner is requested to contact the undersigned attorney at 215-568-3100.

Respectfully submitted,



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